

# PEARSE (H. S.)

SALOPHEN IN ACUTE  
ARTICULAR RHEUMATISM.

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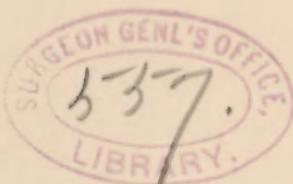
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## SALOPHEN IN ACUTE ARTICULAR RHEUMATISM.

BY HARRY S. PEARSE, M. D.,  
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SINCE 1875, when Buss and Reiss first began to use salicylic acid in rheumatism, the disease has been effectually controlled. After its discovery in 1838 it was used as an antipyretic, and it is presumable that in its employment against the high temperatures of rheumatism these physicians hit upon its happy specific action in this disease. It revolutionized the treatment of rheumatism, and for twenty years salicylic acid, pure and in different combinations, has been the mainstay of the physician.

It did not, however, take the observing members of the profession long to learn that the acid could not be given with impunity. Protracted and energetic use of it was found to produce intense gastric irritation, renal congestion, and even acute parenchymatous nephritis, severe cardiac depression, and acute delirium.

The toxic and irritating effects of the acid, ingested in the pure state, led to the use of combinations, and stimulated the chemists to find one devoid of poisonous qualities, but quite as energetic in its action. Salicylate of so-

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dium was found less irritating to the gastric and intestinal mucous membranes, but did produce delirium, albuminuria, and severe depression. Oil of gaultheria had all the disadvantages of the pure acid when given in sufficient antirheumatic doses. Salol, the phenic ether of salicylic acid, was too expensive, and also productive of renal irritation. Broken up in the intestine into phenic and salicylic elements, the former produced carboluria and often albuminuria. The latest and perhaps the most satisfactory compound is "salophen," obtained by treating paranitrophenol with salicylic acid. It was discovered in 1891 by Bayer, and its physiological actions were worked out and promulgated in that and the succeeding year by Siebel. He found that it required an alkaline medium for its decomposition, and that it was therefore insoluble in the gastric juices, but freely soluble in the intestinal fluids. It decomposed in the intestine into salicylic acid, of which it contained fifty per cent., and acetylpara-amidophenol; the decomposition, a slow one, placed the irritating effect of the acid at nil and the acetylpara-amidophenol, combining with a radicle, formed an insoluble compound.

It would seem upon first thought that this would do away with the toxic principles found so objectionable in the other compounds, and, indeed, clinical employment of the drug has proved this almost beyond a doubt.

As stated above, salicylic acid and its salts have been considered specifics in acute articular rheumatism, and from 1875 to 1892 it was routine work in hospitals and private practice to start the treatment of each case with this drug. Since 1892 it has gradually become routine in practice, especially in hospital work, to start with salophen.

When I was house physician in Bellevue Hospital in 1895, under Dr. Dana, Dr. Fowler, and Dr. Lambert, that was my rule, as indeed it was the custom of all the house

physicians upon the same division dating back into 1892, excluding 1894, which will be explained farther on. Of twenty-three cases that came under my observation, seventeen were acute, two subacute, and four chronic in character. Salophen was used in fourteen of the seventeen acute cases, and in the following synopsis of these, with the conclusions drawn from them, I can only supplement the excellent clinical report of ten cases in the same wards in 1892 and 1893 by Dr. D. B. Hardenbergh.\* In the three remaining acute cases salicylate of sodium was used exclusively, with good results in two and fair results in one. In the subacute and chronic forms iodide of potassium, wine of colchicum, iron, arsenic, and strychnine were employed.

CASE I.—O. B., admitted August 19th; draughtsman, aged twenty-eight years. History of previous attacks. Pain, redness, swelling, and tenderness of left knee. Temperature, 101°·2; pulse, 94; respiration, 24.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours; a five-per-cent. solution of menthol in alcohol to the affected joint.

*August 20th.*—Temperature, pulse, and respiration normal.

*25th.*—Discharged, cured.

CASE II.—J. W., admitted May 3d; accountant, aged thirty-six. History of previous attacks. Attack previous to present one accompanied by acute amygdalitis; present one by slight amygdalitis also. Stiffness, redness, swelling, and pain in both wrists, ankles, and knees. Attack severe. Temperature, 103°; pulse, 96; respiration, 20.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours; Epsom salts as a cathartic; sodium bromide as a hypnotic; menthol dressing to joints.

\* Salophen in Acute Articular Rheumatism, *Med. Record*, July 29, 1893.

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*May 8th.*—Menthol dressings removed. Joint symptoms less severe. Temperature, pulse, and respiration normal.

*14th.*—Cured. Patient remained in the ward as a helper. No recurrence of attacks. Use of salophen continued for a month.

CASE III.—J. P., admitted June 3d; laborer, aged thirty years. No previous attacks. Both knee joints affected. Intense pain. Restlessness. Temperature, 102°; pulse, 96; respiration, 26.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours; U. S. solution of morphine, two drachms at night as a narcotic; menthol dressing to joints.

*June 7th.*—Temperature, pulse, and respiration normal. Sodium bromide substituted for the morphine; rheumatic ointment (salicylic acid, oil of turpentine, lanolin, of each three drachms; lard, three ounces) for menthol dressing.

*June 17th.*—Discharged, cured.

CASE IV.—G. S., admitted June 30th; bartender, aged thirty-three years. History of previous attacks. Wrist and knee joints affected. Highest temperature, pulse, and respiration (second day after admission), 104·2°, 108, and 24.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours; menthol dressing to joints.

*July 4th.*—Temperature, pulse, and respiration normal.

*11th.*—Discharged, cured.

CASE V.—T. H., admitted May 1st; laborer, aged twenty-five years. No previous attacks. Left knee affected. Temperature, 102·6°; pulse, 108; respiration, 24.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours; menthol dressing to joint.

*May 4th.*—Temperature, pulse, and respiration normal.

*9th.*—Discharged, cured.

CASE VI.—J. W., admitted March 29th; minor, aged twelve years. No previous attacks. Left knee affected—

some effusion. Intense pain. Temperature, 105·2°; pulse, 140; respiration, 34.

*Treatment.*—Salophen, ten grains; bicarbonate of sodium, fifteen grains, every four hours; menthol dressing to joint.

*March 30th.*—9 A.M., temperature, 102·6°; pulse, 108; respiration, 26. 9 P.M., temperature, 105·6°; pulse, 134; respiration, 36.

Restlessness and slight delirium, due to hyperpyrexia.

*31st.*—Salicylate of sodium, ten grains every four hours, substituted for salophen.

*April 1st.*—Temperature, pulse, and respiration normal.

*11th.*—Local and general symptoms returned after a remission of five or six days, with a temperature curve septic in character. Gradual swelling of knee with fluctuation. Aspiration showed purulent fluid. Patient transferred to surgical ward, knee opened and drained.

**CASE VII.**—A. B., admitted May 9th; laborer, aged thirty-five years. No previous attacks. Hands, knees, and wrists affected. Temperature, 103·6°; pulse, 84; respiration, 24.

*Treatment.*—Salicylate of sodium, twenty grains; bicarbonate of sodium, twenty grains, every four hours.

*May 13th.*—Salicylate of sodium, five grains every two hours; menthol dressing to joints.

*22d.*—Temperature, 102·8°; pulse, 84; respiration, 20. No abatement of symptoms, either local or general. Salophen, fifteen grains every four hours, substituted for salicylate of sodium. Bromide of sodium as a sedative and hypnotic.

*26th.*—Temperature, pulse, and respiration normal. Subsidence of symptoms.

*June 26th.*—Discharged, cured.

**CASE VIII.**—J. T., admitted June 30th; laborer, aged thirty years. No previous attacks. Attack slight. Right ankle affected. Temperature, 100·4°; pulse, 100; respiration, 24.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours.

*July 3d.*—Temperature, pulse, and respiration normal. Transferred. Convalescent.

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CASE IX.—J. T., admitted July 23d; laborer, aged twenty-six years. No previous attacks. Present attack slight. Temperature,  $101\cdot2^{\circ}$ ; pulse, 76; respiration, 20.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours.

*July 24th.*—Temperature, pulse, and respiration normal.

*29th.*—Transferred. Convalescent.

CASE X.—A. R., admitted August 8th; laborer, aged twenty-four years. No previous attacks. Local and general symptoms well marked. Knee, ankle, and elbow joints affected. Considerable effusion in left knee and elbow. Temperature,  $104\cdot4^{\circ}$ ; pulse, 128; respiration, 30.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours. Sponge compress (sponges wet with five-per-cent. menthol solution) to left knee and elbow. Menthol dressing to other affected joints.

*August 14th.*—Temperature, pulse, and respiration normal. Acute symptoms subsided.

*23d.*—Discharged, cured.

CASE XI.—F. L., admitted June 7th; seamstress, aged twenty-one years. Previous attacks. Wrist and ankle joints affected. Attack severe. Temperature,  $102\cdot8^{\circ}$ ; pulse, 100; respiration, 28.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours. Bromide of sodium as a sedative. Rheumatic ointment to joints.

*June 11th.*—Temperature, pulse, and respiration normal. Local symptoms less severe.

*16th.*—Discharged, cured.

CASE XII.—M. S., admitted August 24th; laborer; aged thirty-six years. No previous attacks. Left knee affected. Local symptoms severe. Temperature,  $103\cdot2^{\circ}$ ; pulse, 112; respiration, 26.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours.

*August 27th.*—Acute symptoms have subsided.

*30th.*—Temperature, pulse, and respiration normal.

*September 5th.*—Discharged, cured.

CASE XIII.—M. H., admitted March 25th; servant, aged eighteen years. No previous attacks. Local symptoms severe. Ankle, knee, and wrist joints affected. Temperature, 100°; pulse, 80; respiration, 20.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours; menthol dressing to joints.

*March 30th.*—No improvement. Salicylate of sodium, fifteen grains every four hours, substituted for salophen.

*April 9th.*—No improvement. Temperature, 100·4°; pulse, 84; respiration, 24. Complained of headache.

*15th.*—No improvement. Oil of gaultheria, ten minims every four hours, substituted for salicylate of sodium; rheumatic ointment for menthol dressing.

*15th.*—Severe headache. Dullness of intellect. œdema of legs. Pain in left side. Well-marked aortic regurgitant murmur. Diminished quantity of urine, which was of high specific gravity, contained a diminished amount of urea with renal epithelium. Intense dyspnoea. Gaultheria stopped, patient put upon the use of digitalis, diuretics, and diaforetics.

*28th.*—Acute renal and cardiac symptoms have subsided. Urine normal.

*May 4th.*—Patient convalescent.

*15th.*—Discharged, cured.

CASE XIV.—A. L., admitted May 2d; servant, aged eighteen. No previous attacks. Local and general symptoms very severe. Knee, ankle, and wrist joints affected. Temperature, 103°; pulse, 102; respiration, 28.

*Treatment.*—Salophen, fifteen grains; bicarbonate of sodium, fifteen grains, every four hours. Bromide of sodium as sedative. Menthol dressing to joints.

*May 6th.*—No improvement. Salicylate of sodium, fifteen grains, substituted for salophen, and rheumatic ointment for menthol dressing.

*11th.*—Violent acute delirium. Salicylate of sodium discontinued. Magendie's solution necessary. Use of salophen resumed.

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18th.—No improvement. Salicylate of sodium again tried, producing acute delirium as before. Alkaline treatment tried.

24th.—No improvement. Advent of acute endocarditis and pericarditis, with septic condition and temperature of 105·8°.

31st.—Since last note a septic state has prevailed. No improvement in the heart. Patient has been comatose most of the time, and died to-day.

A review of these cases warrants some interesting deductions. Considering the first twelve cases excluding the last two on the ground that the temperature was produced by other factors than acute articular rheumatism, the average duration of fever after beginning to use salophen was five days. According to Dr. Whipman,\* in the treatment of one hundred and seventy three cases with the salicylates, the average duration of fever was 8·65 days. In one hundred and ninety cases collected by Wardner the average was 5·5 days; in one hundred and fifty six cases by Owen, 3·66 days; in fifty five cases, according to Howard in Pepper's *System*, 7·25 days; in ten by Hardenbergh, 6·11 days, treated exclusively by salophen.

According to Whipman, in one hundred and sixty-seven cases treated with the salicylates the average duration of the whole attack was 19·03 days; ten by Hardenbergh, using salophen, gave an average of ten days. In my series of twelve the average was 10·25 days. This conclusion is perhaps valueless because of the necessity of transferring some of the patients to another hospital in early convalescence to make room for incoming patients.

The average daily amount given was a drachm and a half in fifteen-grain doses every four hours. This could

\* Report of the Collective Investigation Committee of the British Medical Association.

be continued indefinitely with no untoward effects. One patient took fifteen grains every four hours during the day for a month. With each fifteen grains of salophen, fifteen or twenty grains of bicarbonate of sodium were combined. Led by the fact that there is less probability of cardiac complications in the alkaline treatment than in any other, Dr. Flint advised the combination of the alkaline with the salicylate treatment. The same principle was followed in the use of salophen.

There were no symptoms of gastric irritation, cardiac depression, or renal or cerebral involvement in any one of the salophen cases which could be attributed directly to salophen. On the other hand, I believe that the severe acute renal congestion in Case XIII was directly attributable to the salicylate treatment, and in Case XIV upon two occasions the administration of sodium salicylate was followed by an intense acute delirium. This case was an unusual one, and no antirheumatic treatment would subjugate the intense infection. The fatal cardiac complications, with the hyperpyrexia which developed, can be accounted for by the virulence of the poison, the susceptibility of the patient, and the signal failure of all antirheumatic measures. Dr. Dana considered that a septic element was present, and made the statement that little could be done for severe septic cases.

I do not mean to underestimate the value of the salicylate treatment; vast clinical researches have proved its great worth, but we are all compelled to recognize the dangers attending its careless use. If salophen will act as well in a prolonged and thorough trial as it has in my small series, and continue devoid of dangerous properties, it will eventually replace completely more dangerous methods of treatment.

For the following table of the consumption of the four

## 10 SALOPHEN IN ACUTE ARTICULAR RHEUMATISM.

leading antirrheumatics in Bellevue Hospital since the advent of salophen, I am gratefully indebted to Dr. Charles Rice, chemist to the Department of Public Charities in New York:

	1892.	1893.	1894.	1895.
Acid salicylic.....lbs.	93	157	12·5	170
Sodium salicylate.....lbs.	83	87	56	60
Salophen .....oz.	8	175	None.	430
Oil of gaultheria .....lbs.	18	27½	16¾	22

To use the doctor's words: "These figures are remarkable. It seems as if in 1894 rheumatism had been quite rare. Or else some other treatment was used."

The broad sphere of usefulness of the acid in subacute cases, in the form of ointments and as an antiseptic, accounts for the large amount used.

The field of employment of salophen in Bellevue has been confined pretty closely to acute rheumatic cases, and the increase in the amount used seems to bear testimony to its growing favor.





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FRANK P. FOSTER, M.D.

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THE PHYSICIAN who would keep abreast with the advances in medical science must read a *live* weekly medical journal, in which scientific facts are presented in a clear manner; one for which the articles are written by men of learning, and by those who are good and accurate observers; a journal that is stripped of every feature irrelevant to medical science, and gives evidence of being carefully and conscientiously edited; one that bears upon every page the stamp of desire to elevate the standard of the profession of medicine. Such a journal fulfills its mission—that of educator—to the highest degree, for not only does it inform its readers of all that is new in theory and practice, but, by means of its correct editing, instructs them in the very important yet much-neglected art of expressing their thoughts and ideas in a clear and correct manner. Too much stress can not be laid upon this feature, so utterly ignored by the "average" medical periodical.

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